The Relationship between Diabetic Retinopathy, Glycemic Control, Risk Factor Indicators and Patient Education

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Abstract

Background: Hyperglycemia, high blood pressure and hypercholesterolemia are risk factors for diabetic retinopathy and vision loss in diabetic patients.

Objectives: To evaluate risk factors in patients treated for diabetic retinopathy in our hospital clinic and assess patients' awareness of the impact of glycemic control; and to compare the findings with those in patients followed in a community clinic.

Methods: We performed a cross-sectional comparative study that included 178 consecutive patients with type 2 diabetes mellitus treated in the Retinal Vascular Service of Rabin Medical Center from 1 September to 31 December 2004, and 107 consecutive patients with type 2 diabetes mellitus examined in a community clinic during the same period. A questionnaire was completed; the main outcome measures were glycemic and risk factor control and their correlation with diabetic retinopathy and visual acuity.

Results: Although only 43% of the patients had heard of HbA1c, 98% of them had undergone this analysis, with a mean level of 8.2% (SD 1.9) in the hospital patients and 7.7% (SD 1.6) in the community patients ($P = 0.01$, t-test). HbA1c was lower in hospital patients who were aware of the test. Correlations were found for visual acuity, diabetic retinopathy and laser treatment with HbA1c ≤ 7%, cholesterol level < 200 mg/dl and blood pressure < 130/85 mmHg.

Conclusions: Since our study and previous reports have shown that HbA1c level ≤ 7%, serum cholesterol level < 200 mg/dl and blood pressure < 130/85 mmHg are associated with better preservation of vision in patients with type 2 diabetes mellitus, we propose that the ophthalmologist has a role in educating patients about glucose, lipid and blood pressure control as part of the treatment of diabetic retinopathy.

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Diabetic retinopathy is the leading cause of new cases of blindness in adults aged 20–74 and is responsible for 8% of all cases of legal blindness in the United States [1]. In Israel, DR is the leading cause of new cases of blindness in adults aged 19–80, and it accounts for 14.8% of new blindness certificates issued during 2004 [2]. Several studies have identified risk factors for DR and vision loss, including hyperglycemia, high blood pressure and hypercholesterolemia [3-7]. Accordingly, glycemic control with a reduction of HbA1c to 7% was found to be associated with decreased development and progression of DR in patients with type 1 diabetes mellitus [8-10], as well as a reduction in microvascular endpoints, including the need for retinal laser photocoagulation, in patients with type 2 DM [11]. Blood pressure control was found to have similar effects on the incidence of microvascular complications in type 2 DM. Moreover, a recent study showed that persistent diabetic macular edema following focal laser treatment was associated with elevated HbA1c [12].

The purpose of the present study was to evaluate risk factors in patients treated for DR in our university hospital-based outpatient retinal vascular clinic. These included glycemic control, BP, serum cholesterol and lipid levels, and systemic micro- and macrovascular complications. We also assessed patients' knowledge of their own glycemic control and compared the findings to those in patients with type 2 DM followed in a community-based general ophthalmology clinic.

Patients and Methods

The study was approved by the Rabin Medical Center Institutional Review Board, and informed consent forms were signed by the patients. All consecutive patients with type 2 DM treated and followed in the Retinal Vascular Service of Rabin Medical Center from 1 September to 31 December 2004 were enrolled in the study. A parallel arm of the study included all consecutive patients with type 2 DM examined by a single ophthalmologist (M.G.) in a community-based general ophthalmology clinic during the same period. A detailed questionnaire was completed for each patient, including gender; age; duration of DM; treatment of DM (insulin versus tablets); family history of DM; smoking; patient's acquaintance with HbA1c; patient's knowledge of last HbA1c level; treating physician (family doctor versus endocri-

DR = diabetic retinopathy

DM = diabetes mellitus
BP = blood pressure

nologist); history and treatment of hypertension; treatment with angiotensin-converting enzyme inhibitors; history and treatment of hypercholesterolemia or hyperlipidemia; last documented levels of HbA1c, serum glucose, cholesterol, lipids (within the previous 6 months); and other micro- and macrovascular complications, including nephropathy, ischemic heart disease, cerebrovascular complications and peripheral vascular disease. The data were obtained from patient interviews and review of the electronic central patient repository. The laboratory data were retrieved from the electronic central patient repository of Clalit Health Services (the largest of the four health management organizations in Israel). The patients were tested in different laboratories, according to their place of residence; all these laboratories have the same normal values for the relevant tests.

All patients then underwent a full ophthalmologic examination as well as fluorescein angiography, and the data were added to the questionnaire: best corrected Snellen visual acuity, intraocular pressure, presence of iris neovascularization, lens status, vitreous status, and findings on fundus evaluation – including optic nerve, macula, and diabetic retinopathy status. The latter was divided into proliferative diabetic retinopathy and non-proliferative diabetic retinopathy. Information concerning laser treatment, including panretinal photocoagulation and focal macular treatment, was entered as well. BP was measured in the hospital patients but not in the community patients.

Statistical analysis was performed using SAS/STAT softwear for Windows (2003, SAS, NC, USA). Students *t*-test, Fisher's exact test, Pearson's correlation analysis (ratio or interval scale), and Spearman's correlation analysis (rank) were performed as appropriate.

Results

The sample included 178 patients with type 2 DM treated in the Retinal Vascular Service of Rabin Medical Center (hospital group) and 107 patients with type 2 DM examined in the community-based general ophthalmology clinic (community group). During the study period five hospital patients were not enrolled in the study because of lack of cooperation or consent.

The demographic characteristics of the two groups are presented in Table 1. The hospital patients had a younger mean age than the community patients and a longer duration of diabetes (17.4 ± 8.5 years versus 12.1 ± 10 years, $P < 0.001$, Student's *t*-test) [Table 1]. A larger proportion of the hospital patients were treated by an endocrinologist (rather than solely by the family physician), and a larger proportion were treated with insulin. As expected, DR was noted in 100% of the hospital patients (all of whom were referred to the Retinal Vascular Service) but in only 27 of the 107 community patients. Among the hospital patients, 60% (107/178) had non-proliferative diabetic retinopathy and 40% (71/178) had proliferative diabetic retinopathy. Among the community patients, 70% (19/27) had non-proliferative diabetic retinopathy and 30% (8/27) had proliferative diabetic retinopathy. Laser treatment was delivered to 80% of the hospital patients versus 15% of the community patients.

Table 2 shows the cardiovascular risk factors and their treatment in both groups. The majority of patients received lipid- and hypertension-lowering medications, as well as ACE inhibitors. Mean cholesterol level was < 200 mg/ml in both groups and the lipid levels were well controlled.

Table 3 demonstrates the non-ophthalmic vascular complications in the two groups. The hospital patients had more ischemic heart disease, cerebrovascular disease and proteinuria than the community patients. There was no statistically significant difference in the rate of peripheral vascular disease between the groups.

BP measurement was available only for the hospital patients since BP is not routinely measured in the ophthalmology community clinic. Mean systolic and diastolic BP was 140 ± 22 and 77 ± 12 mmHg, respectively; 45% of the patients had a systolic blood pressure < 130 mmHg and 80% had a diastolic blood pressure < 85 mmHg. Although only 43% of patients in both groups had heard of HbA1c, 98% and 100% of the hospital and community patients, respectively, had undergone this blood test. HbA1c was higher in the hospital group than in the community group (8.2 SD 1.9% vs. 7.7 SD 1.6%, $P = 0.01$, *t*-test), as was the last fasting glucose measurement (171 SD 72 vs. 149 SD 51 mg/dl, $P = 0.004$, *t*-test). Only 29% of the hospital patients and 35% of the community patients had HbA1c ≤ 7%. Among

Table 1. Demographic and treatment characteristics

Parameter	Hospital group	Community group	*P*
Age+ (yrs) mean (SD)	64.8 (9)	68.5 (9.3)	0.001*
Females***	47%	57%	0.9**
Duration of DM (yrs) mean (SD)	17.4 (8.5)	12.1 (10)	< 0.001*
Diabetic retinopathy			
Rate of occurrence	100% (178/178)	25% (27/107)	0.9*
Duration (yrs) mean (SD)	4.1 (4.1)	4.4 (5.4)	
Insulin treatment	48% (84/176)	14% (15/105)	< 0.001**
Endocrinologist	58% (102/176)	24% (24/102)	0.07**

* Student's *t*-test

** Fisher's exact test

*** Data apply to whole group: n = 178 hospital patients and 107 community patients

Table 2. Cardiovascular risk factors and their treatment

Parameter	Hospital group	Community group	*P*
Cholesterol level (mg/dl), mean (SD)	181 (37)	179 (37)	0.99*
LDL cholesterol < 130 mg/dl	81% (138/170)	79% (82/104)	0.90**
Cholesterol < 200 mg/dl	74%(127/171)	72% (77/107)	0.34**
Triglyceride level mean (mg/dl) (SD)	160 (109)	159 (134)	0.99*
Hypertension	69% (121/176)	67% (70/105)	0.83**
Hypertension treatment	61% (105/171)	59% (62/105)	0.72**
Smoking	15% (26/178)	11% (12/105)	0.26**
ACE inhibitors	60% (105/175)	62% (64/103)	0.74**

* Student's t-test

** Fisher's exact test

ACE = angiotensin-converting enzyme

Table 3. Non-ophthalmic vascular complications

Parameter	Hospital group	Community group	*P*
Ischemic heart disease	36% (61/170)	16% (16/101)	0.004*
Cardiovascular disease	15% (26/170)	4% (4/102)	< 0.001*
Peripheral vascular disease	17% (29/170)	13% (13/102)	0.2*
Proteinuria	48% (66/138)	13% (13/97)	< 0.001*

* Fisher's exact test

Table 4. Visual acuity, diabetic retinopathy and laser treatment correlations*

	Hospital group			Community group		
	VA	DR	Laser	VA	DR	Laser
HbA1c ≤ 7% mg/dl	0.24	0.36	0.46	0.31	0.49	0.60
Cholesterol < 200 mg/dl	0.36	0.48	0.57	0.43	0.65	0.77
Diastolic < 85 mmHg	0.21	0.56	0.47	–	–	–
Systolic < 130 mmHg	0.24	0.56	0.35	–	–	–

* Spearman rank correlation $P < 0.05$

VA = Snellen visual acuity.

the hospital patients the HbA1c level was significantly lower in patients aware of HbA1c, as compared to patients who were unaware of the test (7.8 SD 1.6% vs. 8.5 SD 1.2%, respectively, $P = 0.007$, *t*-test). Among the community patients, the HbA1c levels were 7.6 SD 1.2% in patients aware of the test, vs. 7.7 SD 1.8% in unaware patients ($P = 0.6$, *t*-test).

Table 4 summarizes the correlations of HbA1c, cholesterol level and BP with visual acuity, DR and laser treatment. Correlations were found for HbA1c ≤ 7%, cholesterol < 200 mg/dl, diastolic BP < 85 mmHg, and systolic BP < 130 mmHg, with visual acuity, DR and laser treatment. There was no statistically significant difference between the visual acuity of the right and left eyes in all patients

Discussion

This prospective cross-sectional study conducted simultaneously in a university-based retinal vascular service and a community-based general ophthalmology clinic has several important findings that may be of interest to ophthalmologists, endocrinologists and primary care physicians. Although the hospital patients were younger than the community patients, they had longer duration of diabetes and more cardiovascular, cerebrovascular and renal complications. In addition, a larger proportion of the hospital patients were treated with insulin. These observations confirm the impact of early onset, severity and longer duration of DM on the development of DR shown in previous larger population-based and longitudinal studies [4,13].

Only 43% of the patients in the hospital and community groups had heard of HbA1c, although 98% and 100%, respectively, were tested for this factor. This observation indicates insufficient patient education on glycemic control. HbA1c was higher in the hospital group than the community group, as was the last fasting serum glucose level. Only 29% of the hospital patients and 35% of the community patients had HbA1c ≤ 7%. Moreover, hospital patients who were aware of HbA1c had lower levels of this parameter. We also found a correlation between HbA1c ≤ 7% and visual acuity, laser treatment and DR.

Our study does not represent the true long-term glycemic control of these patients as it was cross-sectional rather than longitudinal, using a single HbA1c value recorded over the preceding 3 months. Nevertheless, the findings agree with previous population-based and longitudinal studies showing that glucose control has an important and persistent effect in reducing diabetic microvascular complications. The Diabetes Control and Complications Trial [8] reported that tight glycemic control prevented the progression of the severity of DR and the development of macular edema in patients with type 1 DM [9,10]. In the UK Prospective Diabetes Study of patients with type 2 DM, there was a 25% reduction in the risk of microvascular complications, including the need for retinal photocoagulation, in the group receiving intensive treatment compared with the conventional treatment group [11]. The Barbados Eye Study found that DR risk increased with each 1% of higher HbA1c at baseline [4].

In a recent retrospective study, a correlation was found between persistent clinically significant macular edema and HbA1c in type 2 diabetic patients. Patients with persistent clinically significant macular edema (despite at least two focal laser treatments) had a mean HbA1c of 8.9%, whereas those with resolved macular edema had a mean Hba1c of 6.7% [12]. This finding is in accordance with our finding of correlation between HbA1c ≤ 7% and visual acuity.

BP measurements were available for the hospital patients only, because BP is not routinely measured in the ophthalmology community clinic. We found a positive correlation of a systolic BP of < 130 mmHg and a diastolic BP of < 85 mmHg with DR, laser treatment and visual acuity. Again, a single BP measurement in a hospital setting does not represent true long-term BP control. However, our correlation findings are in line with larger longitudinal population-based studies. A controlled clinical trial of patients with type 2 DM and hypertension (the UKPDS) demonstrated that tight BP control markedly reduces the risk of both progression of DR and deterioration in visual acuity [14]. In the Barbados eye study, high systolic or diastolic BP increased the risk of DR, whereas anti-hypertensive treatment halved the risk of DR versus no treatment [4]. In our sample, the majority of hospital and community patients were receiving anti-hypertensive drugs as well as ACE inhibitors [Table 1]. Indeed, the mean systolic and diastolic BP in the hospital patients were 140 (SD 22) and 77 (SD 12) mmHg, respectively, similar to the tight pressure control values in the UKPDS study [14].

We found correlations between serum cholesterol < 200 mg/dl and DR, laser treatment and visual acuity [Table 4]. In our sample, serum cholesterol levels were below 200 mg/dl in 74% and 72% of the hospital and community patients, respectively, and mean levels for the groups were also lower at 181 (SD 36) mg/dl and 179 (SD 37) mg/dl, respectively [Table 2]. Although this single cholesterol value may not represent the long-term

UKPDS = UK Prospective Diabetes Study

lipid level of these patients, our correlational findings [Table 4] are in accordance with larger observational and population-based studies. Observational data from the Early Treatment Diabetic Retinopathy Study showed that elevated serum cholesterol level was associated with the risk and severity of hard retinal exudates [6] and doubled the risk of moderate vision loss (decrease of ≥ 3 lines) at 5 years. A similar association with hard retinal exudates was noted in the population-based Wisconsin Epidemiologic Study of Diabetic Retinopathy [7].

In summary, the glycemic level in our sample was not adequately controlled but the BP and lipid levels were relatively well controlled. We propose that blood pressure and lipid control are easier to achieve with the proper administration of medications, as was done by the primary care physicians and endocrinologists treating our patients. Glycemic control, however, depends not only on proper glucose-lowering medications, but also on patient adherence to diet and physical activity programs. The lack of a healthy lifestyle in our sample was further demonstrated by the 15% and 11% rates of smoking in the hospital and community patients, respectively.

A previous randomized prospective community-based study of patients with type 2 DM demonstrated that clinician sharing of the therapeutic responsibility with patients improved glycemic, BP and cholesterol control to the same order of magnitude shown in intensive and standard care groups in larger studies, such as the UKPDS [11,14,15]. The fact that in our cohort only 43% of the patients (in both groups) had heard of HbA1c, although all had undergone this test, points to inadequate patient education and, consequently, insufficient patient responsibility for active participation in the management of their disease. Indeed, hospital patients who were unaware of HbA1c had higher HbA1c levels than those who were aware of this test. We therefore suggest that the ophthalmologist take a more active role in educating patients with DM, since the potential risk of vision loss may motivate them to comply with the recommended lifestyle and medical treatment.

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A man who has never gone to school may steal from a freight car; but if he has a university education he may steal the whole railroad

Theodore Roosevelt (1858-1919), 26th U.S. president